Chen C.
10/068570

FILE 'REGISTRY' ENTERED AT 15:48:07 ON 27 MAY 2004
L1 54 S (STREPTAVIDIN? OR PHOSPHOLIPIDS?)/CN

FILE 'HCAPLUS' ENTERED AT 15:48:22 ON 27 MAY 2004
L1 54 SEA FILE=REGISTRY ABB=ON PLU=ON (STREPTAVIDIN? OR PHOSPHOLIPIDS?)/CN
L2 12606 SEA FILE=HCAPLUS ABB=ON PLU=ON LANGMUIR BLODGETT? OR LB(S)LANGMUIR
L3 190 SEA FILE=HCAPLUS ABB=ON PLU=ON L2 AND LIGAND
L4 29 SEA FILE=HCAPLUS ABB=ON PLU=ON L3 AND (POLYPEPTIDE OR PEPTIDE OR PROTEIN OR POLYPROTEIN)
L5 5 SEA FILE=HCAPLUS ABB=ON PLU=ON L4 AND (L1 OR STREPTAVIDIN OR PHOSPHOLIPID OR PHOSPHO LIPID OR PHOSPHATIDE)

L5 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 21 Mar 2004
ACCESSION NUMBER: 2004:223818 HCAPLUS
TITLE: Oriented **protein** immobilization in arrays of surface nanopores
AUTHOR(S): Nguyen, Doris; Bandyopadhyay, Krisanu; Tan, Johannes; Niemz, Angelika; Baker, Shenda M.
CORPORATE SOURCE: Bioengineering, Keck Graduate Institute, Claremont, CA, 91711, USA
SOURCE: Abstracts of Papers, 227th ACS National Meeting, Anaheim, CA, United States, March 28-April 1, 2004 (2004), COLL-215. American Chemical Society: Washington, D. C.
CODEN: 69FGKM
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB A major goal in nanobiotechnol. is to gain control over the spatial distribution and orientation of single **protein** mols., a goal that has not been achieved to date in the development of **protein** nanoarray technologies. We are exploring a novel approach for the oriented immobilization of **proteins** within arrays of surface nanopores. **Proteins** are ordered in an oriented fashion by self-assembly on a **ligand** containing monolayer at the air-water interface. Surface immobilization of discrete **proteins** in confined surface nanopores is achieved by **Langmuir Blodgett** deposition of this monolayer onto silicon wafers with etched arrays of surface nanopores. We herein report initial results obtained for the model system **streptavidin** - biotin, and are in the process of expanding our studies to the generation of oriented single antibody nanoarrays.

L5 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 16 Aug 2002
ACCESSION NUMBER: 2002:615949 HCAPLUS
DOCUMENT NUMBER: 137:165778
TITLE: **Ligand** sensor devices and uses thereof
INVENTOR(S): Vodyanoy, Vitaly J.; Samoylov, Alexandre M.; Samoylova, Tatiana I.; Pathirana, Suram Therese
PATENT ASSIGNEE(S): Auburn University, USA
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002063280	A1	20020815	WO 2002-US3576	20020206
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003040466	A1	20030227	US 2002-68570	20020206
EP 1364201	A1	20031126	EP 2002-709383	20020206
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 2001-266755P P 20010206
WO 2002-US3576 W 20020206

AB Methods for evaluating the affinity of ≥1 **ligands** for a **peptide** of interest are described which entail identifying the **peptide** of interest (e.g., by in vivo screening); preparing the **peptide** to be coupled to a sensor; preparing the sensor to be coupled to the **peptide**; coupling the **peptide** to the sensor; quantifying the signal output from the sensor; exposing the sensor to ≥1 **ligands**; and quantifying the signal output from the sensor and comparing to the previously obtained signal. **Ligand** sensor devices for carrying out the methods are also described which comprise a sensor comprising a piezoelec. crystal; a coupling composition layer; and a layer essentially comprising a **peptide** of interest on top of the coupling composition layer, whereby the binding of **ligands** to the **peptide** of interest may be detected by a change in the signal output from the sensor. Assays using the devices allow detection of **ligand-peptide** interactions directly in tissue samples and thus provide an in vitro assay to characterize **peptides ligands**. The methods and apparatus find particular use in characterizing cell-specific **peptides** isolated from in vivo screening in animals to determine their suitability for use in human therapy.

IT **9013-20-1, Streptavidin**
RL: ARU (Analytical role, unclassified); DEV (Device component use); ANST (Analytical study); USES (Uses)
(**ligand** sensor devices and their use)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 19 Mar 2002

ACCESSION NUMBER: 2002:205117 HCAPLUS
DOCUMENT NUMBER: 137:365669
TITLE: Supported lipid membranes for reconstitution of membrane **proteins**
AUTHOR(S): Lindholm-Sethson, Britta
CORPORATE SOURCE: Department of Chemistry, Analytical Chemistry, Umea University, Umea, SE - 901 87, Swed.
SOURCE: Focus on Biotechnology (2001), 7(Physics and Chemistry: Basis of Biotechnology), 131-165
CODEN: FBOIAM
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Various methods for creation of supported lipid membranes suitable for incorporation of membrane **proteins** are described, including **Langmuir-Blodgett** techniques, self-assembly of thiolipids and/or **phospholipids** and fusion of vesicles. Practical applications that are discussed include **ligand**-receptor binding, immunosensing devices, membrane fluidity, ion-selective sensors and signal transduction from reconstituted membrane **proteins**.
REFERENCE COUNT: 143 THERE ARE 143 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 15 Oct 2000
ACCESSION NUMBER: 2000:726665 HCAPLUS
DOCUMENT NUMBER: 134:127554
TITLE: Characterization of the interactions between various hexadecylmannoside-**phospholipid** model membranes with the lectin concanavalin A
AUTHOR(S): Bakowsky, Udo; Rettig, Willi; Bendas, Gerd; Vogel, Jan; Bakowsky, Heike; Harnagea, Catalin; Rothe, Ulrich
CORPORATE SOURCE: Department of Physiological Chemistry, University of Groningen, Groningen, Neth.
SOURCE: Physical Chemistry Chemical Physics (2000), 2(20), 4609-4614
CODEN: PPCPFQ; ISSN: 1463-9076
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The specific interaction of Con A with glycolipid-containing model membranes was investigated using (a) surface pressure-time (Π-t) curves, (b) epifluorescence microscopy connected to a film balance, (c) atomic force microscopy (AFM) of the monofilms after **Langmuir-Blodgett** (**LB**) transfer and (d) quartz crystal microbalance (QCMB) weight-quantification of the adhered **protein** on the glycolipid model membrane. The adsorption of Con A on a model membrane was mannose-specific and concentration-dependent in the range 1-50% (1% was the lower detection limit, whereas above 30% saturation began). Adsorption kinetics was followed by QCMB and Π-t measurements. Saturation was reached after 1 h. Hydrophilic spacers were introduced between the alkyl chain and the mannose headgroup of the Con A **ligands**. The quantity of specific

Con A-adhesion increased with spacer length and also the adhesion kinetics was accelerated using protruding **ligands**. With AFM it was possible to detect morphol. differences of mixed hexadecylmannoside-1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC) films in dependence on spacer length of the glycolipid before and after mol. contact with Con A.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 31 Mar 1990
ACCESSION NUMBER: 1990:115062 HCAPLUS
DOCUMENT NUMBER: 112:115062
TITLE: Specific and unspecific binding of concanavalin A at monolayer surfaces
AUTHOR(S): Haas, H.; Moehwald, H.
CORPORATE SOURCE: Inst. Phys. Chem., Univ. Mainz, Mainz, D6500, Fed. Rep. Ger.
SOURCE: Thin Solid Films (1989), 180, 101-10
CODEN: THSFAP; ISSN: 0040-6090
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Fluorescence and electron microscopic studies with **phospholipid** monolayers containing Con A and with or without a glycolipid as a specific **ligand** are presented. It is shown that the (unspecific) **protein** insertion in the absence of the glycolipid leads to **protein** patches that may exhibit uniform sizes and that may be due to the existence of long-range electrostatic forces resulting from a difference in the polarization of different **protein** and lipid areas. By incorporating .apprx.1 mol% of the glycolipid, specific binding can be effected. This can dominate the unspecific process only in a narrow lateral pressure range of 5-15 nM/m. The data can be qual. understood, indicating that control of the interactions requires fine tuning of the head-group arrangement.

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 15:50:01 ON 27 MAY 2004)
L6 10 S L5
L7 10 DUP REM L6 (0 DUPLICATES REMOVED)

L7 ANSWER 1 OF 10 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2002-691574 [74] WPIDS
DOC. NO. NON-CPI: N2002-545604
DOC. NO. CPI: C2002-195421
TITLE: Evaluating affinity of one or more **ligands** for a **peptide** of interest comprises coupling the **peptide** to a sensor, exposing the sensor to **ligands** and quantifying signal output from sensor before and after the exposure.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): PATHIRANA, S T; SAMOYLOV, A M; SAMOYLOVA, T I; VODYANOY, V; VODYANOY, V J
PATENT ASSIGNEE(S): (PATH-I) PATHIRANA S T; (SAMO-I) SAMOYLOV A M;

(SAMO-I) SAMOYLOVA T I; (VODY-I) VODYANOY V; (AUBU) UNIV AUBURN

COUNTRY COUNT: 101

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002063280	A1	20020815	(200274)*	EN	48
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW					
US 2003040466	A1	20030227	(200318)		
EP 1364201	A1	20031126	(200380)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR					
AU 2002243868	A1	20020819	(200427)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002063280	A1	WO 2002-US3576	20020206
US 2003040466	A1 Provisional	US 2001-266755P	20010206
		US 2002-68570	20020206
EP 1364201	A1	EP 2002-709383	20020206
		WO 2002-US3576	20020206
AU 2002243868	A1	AU 2002-243868	20020206

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1364201	A1 Based on	WO 2002063280
AU 2002243868	A1 Based on	WO 2002063280

PRIORITY APPLN. INFO: US 2001-266755P 20010206; US 2002-68570 20020206

AN 2002-691574 [74] WPIDS

AB WO 200263280 A UPAB: 20021118

NOVELTY - Evaluating (M) the affinity of one or more **ligands** for a **peptide** of interest (POI), comprises identifying the POI, preparing the **peptide** to be coupled to a sensor (S), and the S to be coupled to the **peptide**, coupling the **peptide** to S, quantifying the signal output from S, exposing S to one or more **ligands** and quantifying signal output from S and comparing to previously obtained signal.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a **ligand** sensor device (LSD) comprising a sensor comprising a piezoelectric crystal, a coupling composition layer and a layer essentially comprising POI on top of the coupling composition layer, where the binding of **ligands** to POI may be detected by a change in the signal output from the sensor.

USE - (M) is useful for evaluating the affinity of one or more **ligands** for a POI (claimed). The LSD and (M) find particular use in characterizing cell-specific **peptides** isolated from in vivo screening in animals to determine their suitability for use in human therapy, and are also useful in the isolation and identification of tissue-specific molecules that can be used to target various compounds or molecules in gene and/or drug therapy protocols.

ADVANTAGE - (M) allows detection of **ligand-peptide** interactions directly in tissue samples, and the rapid discovery of small molecule **ligands** specific to various organs, tissues and cell types.

DESCRIPTION OF DRAWING(S) - The figure shows the **ligand** sensor device, where the **peptide** of interest is coupled to the sensor by a coupling composition layer comprising **streptavidin**.

Dwg.1/6

L7 ANSWER 2 OF 10 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 2002:337352 SCISEARCH
THE GENUINE ARTICLE: 542AZ
TITLE: Lipid domain formation and **ligand**-receptor distribution in lipid bilayer membranes investigated by atomic force microscopy
AUTHOR: Kaasgaard T; Mouritsen O G; Jorgensen K (Reprint)
CORPORATE SOURCE: Tech Univ Denmark, Dept Chem, DK-2800 Lyngby, Denmark (Reprint); Univ Southern Denmark, MEMPHYS, Ctr Biomembrane Phys, DK-5230 Odense M, Denmark
COUNTRY OF AUTHOR: Denmark
SOURCE: FEBS LETTERS, (27 MAR 2002) Vol. 515, No. 1-3, pp. 29-34.
Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS.
ISSN: 0014-5793.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 39

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB A novel experimental technique, based on atomic force microscopy (AFM), is proposed to visualize the lateral organization of membrane systems in the nanometer range. The technique involves the use of a **ligand**-receptor pair, biotin-avidin, which introduces a height variation on a solid-supported lipid bilayer membrane. This leads to a height amplification of the lateral membrane organization that is large enough to be clearly imaged by scanning AFM. The power of the technique is demonstrated for a binary dipalmitoylphosphocholine-diarachidoylphosphocholine lipid mixture which is shown to exhibit a distinct lateral lipid domain formation. The new and simple **ligand**-receptor-based AFM approach opens up new ways to investigate lipid membrane microstructure in the nanometer range as well as the lateral distribution of **ligand**-lipid and receptor-**protein** complexes in supported membrane systems. (C) 2002 Federation of European Biochemical Societies. Published by Elsevier Science B.V. All rights reserved.

L7 ANSWER 3 OF 10 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 2001:679900 SCISEARCH
THE GENUINE ARTICLE: 464DR
TITLE: Non-specific and specific adsorption of **proteins** on **Langmuir-Blodgett** films of amino acid derivative polymers
AUTHOR: Ide M; Mitamura A; Miyashita T (Reprint)
CORPORATE SOURCE: Tohoku Univ, Inst Multidisciplinary Res Adv Mat, Aoba Ku, 2-1-1 Katahira, Sendai, Miyagi 9808577, Japan (Reprint); Tohoku Univ, Inst Multidisciplinary Res Adv Mat, Aoba Ku, Sendai, Miyagi 9808577, Japan
COUNTRY OF AUTHOR: Japan
SOURCE: BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, (JUL 2001) Vol. 74, No. 7, pp. 1355-1359.
Publisher: CHEMICAL SOC JAPAN, 1-5 KANDA-SURUGADAI CHIYODA-KU, TOKYO, 101, JAPAN.
ISSN: 0009-2673.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 22
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Polymer LB films consisting of lysine and alanine derivative polymers were prepared to investigate the interfacial recognition between **protein** and **ligand** on the LB film. The surface of lysine derivative polymer LB film was modified by the biotin molecule that is the **ligand** for avidin. The biotinylation was carried out without inducing non-specific adsorption of **proteins**; avidin specifically adsorbed onto the biotinylated surfaces. Moreover, it was found that there is an optimum molar ratio of biotinylation for the adsorption of avidin onto the surface.

L7 ANSWER 4 OF 10 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 2000:776339 SCISEARCH
THE GENUINE ARTICLE: 362HL
TITLE: Characterization of the interactions between various hexadecylmannoside-**phospholipid** model membranes with the lectin Concanavalin A
AUTHOR: Bakowsky U (Reprint); Rettig W; Bendas G; Vogel J; Bakowsky H; Harnagea C; Rothe U
CORPORATE SOURCE: UNIV GRONINGEN, DEPT PHYSIOL CHEM, A DEUSINGLAAN 1, NL-9713 AV GRONINGEN, NETHERLANDS (Reprint); UNIV HALLE WITTENBERG, DEPT PHARM, D-06120 HALLE, GERMANY; MAX PLANCK INST MICROSTRUCT PHYS, D-06120 HALLE, GERMANY
COUNTRY OF AUTHOR: NETHERLANDS; GERMANY
SOURCE: PHYSICAL CHEMISTRY CHEMICAL PHYSICS, (2 OCT 2000) Vol. 2, No. 20, pp. 4609-4614.
Publisher: ROYAL SOC CHEMISTRY, THOMAS GRAHAM HOUSE, SCIENCE PARK, MILTON RD, CAMBRIDGE CB4 0WF, CAMBS, ENGLAND.
ISSN: 1463-9076.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: PHYS
LANGUAGE: English

REFERENCE COUNT: 18

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The specific interaction of Concanavalin A (ConA) with glycolipid-containing model membranes was investigated using (a) surface pressure-time (Pi-t) curves, (b) epifluorescence microscopy connected to a film balance, (c) atomic force microscopy (AFM) of the monofilms after **Langmuir-Blodgett** (**LB**) transfer and (d) quartz crystal microbalance (QCMB) weight-quantification of the adhered **protein** on the glycolipid model membrane. The adsorption of ConA on a model membrane was mannose-specific and concentration-dependent in the range 1-50% (1% was the lower detection limit, whereas above 30% saturation began). Adsorption kinetics was followed by QCMB and Pi-t measurements. Saturation was reached after 1 h. Hydrophilic spacers were introduced between the alkyl chain and the mannose headgroup of the ConA **ligands**. The quantity of specific ConA-adhesion increased with spacer length and also the adhesion kinetics was accelerated using protruding **ligands**. With AFM it was possible to detect morphological differences of mixed hexadecylmannoside-1,2-distearyl-sn-glycero-3-phosphocholine (DSPC) films in dependence on spacer length of the glycolipid before and after molecular contact with ConA.

L7 ANSWER 5 OF 10 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 1998:647080 SCISEARCH
THE GENUINE ARTICLE: 112GD
TITLE: Surface-promoted thioether linkage between proto- or hemato porphyrins and thiol-silanized quartz: Formation of self-assembled monolayers and interaction with imidazole and carbon monoxide
AUTHOR: Pilloud D L (Reprint); Moser C C; Reddy K S; Dutton P L
CORPORATE SOURCE: UNIV PENN, SCH MED, DEPT BIOCHEM & BIOPHYS, JOHNSON RES FDN, B501 RICHARDS BLDG, PHILADELPHIA, PA 19104 (Reprint)
COUNTRY OF AUTHOR: USA
SOURCE: LANGMUIR, (18 AUG 1998) Vol. 14, No. 17, pp. 4809-4818.
Publisher: AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036.
ISSN: 0743-7463.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: PHYS
LANGUAGE: English
REFERENCE COUNT: 63

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Free base protoporphyrin IX (PP),(1) Zn(II)protoporphyrin IX (Zn(II)PP), Fe(III)protoporphyrin IX (Fe(III)PP), and Fe(III)protoporphyrin IX dimethylester (Fe(III)PPDME) as well as free base hematoporphyrin were selectively chemisorbed onto thiol-silanized quartz in aqueous media at neutral pH values and at room temperature. The self-assembled monolayers (SAMs) were characterized by UV/vis absorption and fluorescence spectroscopy. Evidence for chemisorption through the formation of thioether linkages between the immobilized thiols at the surface and the vinyl or the hydroxyethyl groups of the porphyrins is as follows: (1) Only

porphyrins that possess either vinyl or hydroxyethyl groups show the characteristic absorption and properties of a SAM; porphyrins free of vinyl or hydroxyethyl groups do not form SAMs. (2) Attachment to the surface through the propionates of the metal is ruled out since the presence of both metal and propionates is not mandatory for the formation of SAMs. (3) None of the porphyrins form SAMs on bare quartz or on quartz silanized with propyltrimethoxysilane. To our knowledge, this is the first description of a direct reaction under physiological conditions between thiols and the vinyl or the hydroxyethyl groups of porphyrin. This is analogous to the covalent attachment of heme in cytochrome c through the poorly understood reaction between the vinyl groups of the heme and the thiol of cysteine. Furthermore, this surface-promoted chemistry provides a simple and direct method for attaching unmodified porphyrins onto solid substrates to form remarkably robust monolayers. Linear dichroism revealed that the Fe(III)PPs in the monolayer are tilted in average at an angle of 33 degrees relative to the substrate, shifting to 46 degrees after ligation to imidazole. Carbon monoxide coordinates to Fe(II) in SAMs of FePP and FePPDME. SAMs of Fe(III)PP and Fe(III)PPDME ligate imidazole cooperatively and, after reduction, bind CO reversibly. In contrast, only one imidazole ligates to Zn(II)PP as a SAM, and no interaction with CO was observed.

L7 ANSWER 6 OF 10 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 97:560401 SCISEARCH
THE GENUINE ARTICLE: XM005
TITLE: Electronic processes in supported bilayer lipid membranes (s-BLMs) containing a geodesic form of carbon (fullerene C-60)
AUTHOR: Tien H T (Reprint); Wang L G; Wang X; Ottova A L
CORPORATE SOURCE: MICHIGAN STATE UNIV, DEPT PHYSIOL, MEMBRANE BIOPHYS LAB, GILTNER HALL, E LANSING, MI 48824 (Reprint); NANKAI UNIV, DEPT PHYS, TIANJIN 300071, PEOPLES R CHINA; SLOVAK TECH UNIV, CTR INTERFACE SCI, DEPT MICROELECT, BRATISLAVA, SLOVAKIA
COUNTRY OF AUTHOR: USA; PEOPLES R CHINA; SLOVAKIA
SOURCE: BIOELECTROCHEMISTRY AND BIOENERGETICS, (MAY 1997) Vol. 42, No. 2, pp. 161-167.
Publisher: ELSEVIER SCIENCE SA LAUSANNE, PO BOX 564, 1001 LAUSANNE, SWITZERLAND.
ISSN: 0302-4598.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 101
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The light-induced voltage and current generated by doping a self-assembled and supported bilayer lipid membrane (s-BLM) with buckminsterfullerene C-60 were investigated. Using these s-BLMs, it is possible to construct sensor probes and to investigate redox reactions and light-induced electron transfer across the lipid bilayer. The C-60-containing s-BLM, considered basically as a ''molecular device'', is a light-sensitive diode capable of photoinduced charge separation which undergoes redox reactions across the substrate-hydrophobic lipid bilayer-aqueous solution

junctions. Using the cyclic voltammetry technique, our results show that C-60 embedded in the BLM acts as an excellent electron carrier/mediator and should be useful for electrochemical biosensor and molecular electronics device development. It is concluded that supported BLMs with excellent stability, possessing the structural and dynamic properties of conventional planar lipid bilayers, are excellent models for investigating basic membrane-mediated **ligand**-receptor contact interactions. For practical applications, the s-BLMs are ideal systems for incorporating a host of compounds, including fullerenes, semiconducting nanoparticles, receptor **proteins** and polymeric materials. (C) 1997 Elsevier Science S.A.

L7 ANSWER 7 OF 10 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 96:12546 SCISEARCH
THE GENUINE ARTICLE: TK285
TITLE: THE SPECIFIC ADSORPTION OF **STREPTAVIDIN** TO A TETRABIOTINYLATED PORPHYRIN MONOLAYER AT THE AIR-WATER-INTERFACE
AUTHOR: FUKUSHIMA H (Reprint); TAYLOR D M; MORGAN H; RINGSDORF H; RUMP E
CORPORATE SOURCE: JRDC, ERATO, PROT ARRAY PROJECT, TSUKUBA, IBARAKI, JAPAN (Reprint); UNIV WALES, INST MOLEC & BIOMOLEC ELECTR, BANGOR LL57 1UT, GWYNEDD, WALES; UNIV GLASGOW, DEPT ELECTR & ELECT ENGN, GLASGOW G12 8LT, LANARK, SCOTLAND; UNIV MAINZ, INST ORGAN CHEM, W-6500 MAINZ, GERMANY
COUNTRY OF AUTHOR: JAPAN; WALES; SCOTLAND; GERMANY
SOURCE: THIN SOLID FILMS, (01 OCT 1995) Vol. 266, No. 2, pp. 289-291.
ISSN: 0040-6090.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: PHYS; ENGI
LANGUAGE: ENGLISH
REFERENCE COUNT: 12
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The specific interaction at the air-water interface between **streptavidin** and a monolayer of the tetrabiotinylated **ligand** 5,10,15,20-tetrakis {alpha-[4-(biotinylamidomethyl)pyridinium bromide]-p-tolyl} porphyrin, stabilised by complexation with sodium octadecyl sulphate, is observed directly by surface pressure measurements and by fluorescence microscopy. Changes in the structure of the monolayer, especially the appearance of domains, after adding **protein** to the subphase confirm that the concomitant expansion of the pressure-area isotherm is caused by the specific adsorption of **protein** to biotin **ligands** in the monolayer.

L7 ANSWER 8 OF 10 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 93:721117 SCISEARCH
THE GENUINE ARTICLE: MH664
TITLE: COOPERATIVITY IN THE BINDING OF AVIDIN TO BIOTIN-LIPID-DOPED **LANGMUIR-BLODGETT**-FILMS
AUTHOR: ZHAO S L; WALKER D S; REICHERT W M (Reprint)
CORPORATE SOURCE: DUKE UNIV, DEPT BIOMED ENGN, DURHAM, NC, 27708; DUKE

UNIV, CTR EMERGING CARDIOVASC TECHNOL, DURHAM, NC, 27708
COUNTRY OF AUTHOR: USA
SOURCE: LANGMUIR, (NOV 1993) Vol. 9, No. 11, pp. 3166-3173.
ISSN: 0743-7463.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: PHYS
LANGUAGE: ENGLISH
REFERENCE COUNT: 31
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Monolayers of arachidic acid (AA) doped with either biotinylated DPPE (B-DPPE) or a chain extended biotinylated DPPE (B-x-DPPE) were deposited onto alkylsilane treated surfaces of quartz evanescent fiber optic sensors (EFO) by the **Langmuir-Blodgett** (**LB**) technique. The surface-modified EFOs were used to obtain binding isotherms of fluorescein-labeled avidin to the biotin-lipid-doped **LB** films. Hyperbolic binding isotherms were observed for all B-DPPE doped **LB** films and for B-x-DPPE doped films with < 0.63 mol % biotin lipid. Sigmoid or positively cooperative binding isotherms were observed for all **LB** films with greater-than-or-equal-to 0.63 mol % B-x-DPPE. A mathematical expression for **protein** binding to a two-dimensional array of receptors that takes **protein-protein** interaction into account was used to quantitatively assess the cooperativity observed in the isotherms. Attenuated total reflection Fourier transform infrared (ATR-FTIR) spectroscopy was used to address speculation that cooperativity resulted from a conformational change in avidin. ATR-FTIR results show that avidin experienced significant conformational changes when bound to biotin lipids in the **LB** films, wheras no conformational change was observed for avidin nonspecifically bound to biotin-free **LB** films.

L7 ANSWER 9 OF 10 MEDLINE on STN
ACCESSION NUMBER: 94004064 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1339495
TITLE: Internal and interfacial structure of membranes studied using X-ray standing waves.
AUTHOR: Caffrey M; Wang J
CORPORATE SOURCE: Department of Chemistry and Chemical Physics Program, Ohio State University, Columbus 43210-1173.
CONTRACT NUMBER: DK 36849 (NIDDK)
SOURCE: Faraday discussions, (1992) (94) 283-93.
Journal code: 9212301. ISSN: 1359-6640.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Space Life Sciences
ENTRY MONTH: 199311
ENTRY DATE: Entered STN: 19940117
Last Updated on STN: 19940117
Entered Medline: 19931123

AB The X-ray standing wave (XSW) method developed in the mid-Sixties was used then to determine the position of heavy atoms in and on crystals of silicon and germanium with sub-Angstrom resolution. The advent of layered synthetic microstructures, used primarily as

wide-bandpass X-ray monochromators, heralded a new era in the use of XSW to study biologically relevant structures with a length scale of the order of tens of Angstroms. The original measurements were performed on model membrane **Langmuir-Blodgett** (**LB**) films and served to establish the utility of the XSW approach in determining heavy-atom location in such systems with sub-Angstrom resolution and in tracking the heavy-atom layer as it moves during a thermotropic transition. Recent measurements show that the XSW is well defined at close to 1000 A from the XSW generating surface. Thus, the useful probing distance of XSW is of this length scale also without a compromise in resolution. In addition to the above measurements on well ordered systems the XSW method is being used to profile ion distribution 'directly' at the membrane/aqueous interface. Recent results show that the diffuse double layer can be established reversibly by suitably adjusting the pH of the aqueous phase next to a **phospholipid** membrane. The advantages and disadvantages of this new surface technique as applied to the study of membrane structure and interfacial phenomena are discussed.

L7 ANSWER 10 OF 10 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 91:483823 SCISEARCH
THE GENUINE ARTICLE: GC484
TITLE: CHARACTERIZATION OF CHEMISORBED MONOLAYERS BY SURFACE-POTENTIAL MEASUREMENTS
AUTHOR: TAYLOR D M (Reprint); MORGAN H; DSILVA C
CORPORATE SOURCE: UNIV WALES, INST MOLEC & BIOMOLEC ELECTR, DEAN ST, BANGOR LL57 1UT, WALES (Reprint)
COUNTRY OF AUTHOR: WALES
SOURCE: JOURNAL OF PHYSICS D-APPLIED PHYSICS, (1991) Vol. 24, No. 8, pp. 1443-1450.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: PHYS
LANGUAGE: ENGLISH
REFERENCE COUNT: 22
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Chemisorption has been used to immobilize uniform, low-defect density monolayers of aminopropylsilane and of d-biotin on evaporated gold substrates. The quality of the monolayers has been confirmed by surface potential measurements and by copper decoration. Avidin has been immobilized to these monolayers by (i) crosslinking to the aminopropylsilane with glutaraldehyde and (ii) binding directly to the biotin **ligand**. The changes in surface potential observed during each immobilization step are shown to be related directly to the molecular structure of each chemisorbed layer. Significantly, when the avidin is immobilized on the biotin monolayer the tetrameric **protein** is orientated with one pair of biotin binding sites on the upper surface of the **protein** monolayer. This allows the bifunctional **ligand**, bisbiotin, to be bound to the **protein** giving the possibility of attaching further **protein** layers to form molecular organizates suitable for molecular electronic and molecular sensing applications.

(FILE 'MEDLINE' ENTERED AT 15:50:46 ON 27 MAY 2004)
L8 119 SEA FILE=MEDLINE ABB=ON PLU=ON (STREPTAVIDIN AND

LIGANDS)/CT
L9 29 SEA FILE=MEDLINE ABB=ON PLU=ON L8 AND (PROTEINS OR PEPTIDES OR POLYPROTEINS)/CT

L9 ANSWER 1 OF 29 MEDLINE on STN
ACCESSION NUMBER: 2004158377 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15051330
TITLE: Contributions to the catalytic efficiency of enzymes, and the binding of ligands to receptors, from improvements in packing within enzymes and receptors.
AUTHOR: Williams Dudley H; Stephens Elaine; Zhou Min; Zerella Rosa
CORPORATE SOURCE: Department of Chemistry, University of Cambridge, England.
SOURCE: Methods in enzymology, (2004) 380 3-19.
Journal code: 0212271. ISSN: 0076-6879.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200405
ENTRY DATE: Entered STN: 20040331
Last Updated on STN: 20040512
Entered Medline: 20040511
ED Entered STN: 20040331
Last Updated on STN: 20040512
Entered Medline: 20040511

L9 ANSWER 2 OF 29 MEDLINE on STN
ACCESSION NUMBER: 2003441702 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14500846
TITLE: DNA display for in vitro selection of diverse peptide libraries.
AUTHOR: Yonezawa Masato; Doi Nobuhide; Kawahashi Yuko; Higashinakagawa Toru; Yanagawa Hiroshi
CORPORATE SOURCE: Department of Biosciences and Informatics, Keio University, Yokohama 223-8522, Japan.
SOURCE: Nucleic acids research, (2003 Oct 1) 31 (19) e118.
Journal code: 0411011. ISSN: 1362-4962.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: (EVALUATION STUDIES)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200310
ENTRY DATE: Entered STN: 20030923
Last Updated on STN: 20031021
Entered Medline: 20031020
ED Entered STN: 20030923
Last Updated on STN: 20031021
Entered Medline: 20031020
AB We describe the use of a DNA display system for in vitro selection of peptide ligands from a large library of peptides displayed on their encoding DNAs. The method permits completely in vitro construction of a DNA-tagged peptide library by using a wheat germ in vitro transcription/translation system compartmentalized in

water-in-oil emulsions. Starting with a library of 10(9)-10(10) random decapeptides, 21 different peptide ligands were isolated for monoclonal antibody anti-FLAG M2. DNA display selected more diverse peptides with a DYKXXD consensus motif than previously reported phage display systems. Binding and recovery rates of three peptides were significantly higher than those of the original FLAG peptide, implying that these peptides would be superior to the FLAG peptide for purification of tagged proteins. The simplicity of DNA display enables two selection rounds per day to be conducted. Further, DNA display can overcome the limitations of previous display technologies by avoiding the use of bacterial cells and RNA tags. Thus, DNA display is expected to be useful for rapid screening of a wide variety of peptide ligands for corresponding receptors.

L9 ANSWER 3 OF 29 MEDLINE on STN
ACCESSION NUMBER: 2003328051 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12857387
TITLE: High-throughput screen for inhibitors of 1-deoxy-d-xylulose 5-phosphate reductoisomerase by surrogate ligand competition.
AUTHOR: Gottlin Elizabeth B; Benson R Edward; Conary Scott; Antonio Brett; Duke Kellie; Payne E Sturgis; Ashraf S Salman; Christensen Dale J
CORPORATE SOURCE: Karo Bio USA, Inc., Durham, NC, USA.
SOURCE: Journal of biomolecular screening : official journal of the Society for Biomolecular Screening, (2003 Jun) 8 (3) 332-9.
Journal code: 9612112. ISSN: 1087-0571.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200402
ENTRY DATE: Entered STN: 20030715
Last Updated on STN: 20040224
Entered Medline: 20040223

ED Entered STN: 20030715
Last Updated on STN: 20040224
Entered Medline: 20040223

AB 1-Deoxy-D-xylulose 5-phosphate reductoisomerase (Dxr) is a key enzyme in a biosynthetic pathway for isoprenoids that is unique to eubacteria and plants. Dxr catalyzes the rearrangement and NADPH-dependent reduction of 1-deoxy-D-xylulose 5-phosphate to 2-C-methyl-D-erythritol 4-phosphate. The authors have purified Escherichia coli Dxr and devised a high-throughput screen (HTS) for compounds that bind to this enzyme at a functional site. Evidence is presented that the surrogate ligand directly binds or allosterically affects both the D-1-deoxyxylulose 5-phosphate (DXP) and NADPH binding sites. Compounds that bind at either or both sites that compete for binding with the surrogate ligand register as hits. The time-resolved fluorescence-based assay represents an improvement over the Dxr enzyme assay that relies on relatively insensitive measurements of NADPH oxidation. Screening 32,000 compounds from a diverse historical library, the authors obtained 89 potent inhibitors in the surrogate ligand competition assay. The results presented here suggest that peptide surrogate ligands may be

useful in formatting HTS for proteins with difficult biochemical assays or targets of unknown function.

L9 ANSWER 4 OF 29 MEDLINE on STN
ACCESSION NUMBER: 2003328049 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12857385
TITLE: Biotinylated synthetic chemokines: their use for the development of nonradioactive whole-cell binding assays.
AUTHOR: Thierry Anne-Christine; Perrenoud Genevieve; Pinaud Stephane; Bigler Nicolas; Denis Berangere; Roggero Mario; Moulon Corinne; Demotz Stephane
CORPORATE SOURCE: Dictagene, Lausanne, Switzerland.
SOURCE: Journal of biomolecular screening : official journal of the Society for Biomolecular Screening, (2003 Jun) 8 (3) 316-23.
Journal code: 9612112. ISSN: 1087-0571.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200402
ENTRY DATE: Entered STN: 20030715
Last Updated on STN: 20040224
Entered Medline: 20040223

ED Entered STN: 20030715
Last Updated on STN: 20040224
Entered Medline: 20040223

AB A chemokine binding assay on whole cells was developed using biotinylated synthetic CCL22 as a model ligand. CCL22 analogues were produced by a chemical route, resulting in > 97% homogeneous and defined polypeptides. First, the 5 biotinylated CCL22 analogues synthesized were captured by agarose-immobilized streptavidin, indicating that the biotin molecules introduced in positions G1, K27, K49, K61, and K66 of CCL22 were accessible for binding. Then, it was established using a migration assay that the biotinylated chemokines were at least as biologically active as the unmodified CCL22 form. Subsequently, the biotinylated chemokines were evaluated in an FACS-based whole-cell binding assay. Surprisingly, only the CCL22 analogue with the biotin in position K66 constituted a suitable staining reagent for CCR4-positive cells. Finally, binding characteristics and reproducibility of the binding assay were outlined for the CCL22 analogue with the biotin in position K66. These results exemplified that biotinylated synthetic chemokines constitute promising ligands for the development of chemokine receptor-binding assays on whole cells, provided the position of the biotin moiety introduced along the sequence is adequately chosen.

L9 ANSWER 5 OF 29 MEDLINE on STN
ACCESSION NUMBER: 2003236098 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12758085
TITLE: Ligand binding energy and catalytic efficiency from improved packing within receptors and enzymes.
AUTHOR: Williams Dudley H; Stephens Elaine; Zhou Min
CORPORATE SOURCE: Department of Chemistry, University of Cambridge,

UK.. dhw1@cam.ac.uk
SOURCE: Journal of molecular biology, (2003 May 30) 329 (2) 389-99.
Journal code: 2985088R. ISSN: 0022-2836.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200306
ENTRY DATE: Entered STN: 20030522
Last Updated on STN: 20030627
Entered Medline: 20030626

ED Entered STN: 20030522
Last Updated on STN: 20030627
Entered Medline: 20030626

AB Some small molecules bind to their receptors, and transition states to enzymes, so strongly as to defy current understanding. We show that in the binding of biotin to streptavidin, the streptavidin structure becomes better packed. We conclude that this contraction of the streptavidin structure promotes biotin binding. The improved packing is associated with positively cooperative binding, occurring with a benefit in enthalpy and a cost in entropy. Evidence indicating that catalytic efficiency can also originate via improved packing in some enzyme transition states, derived from the work of others, is presented. Negatively cooperative ligand binding is concluded to induce converse effects (less efficient packing, a cost in enthalpy, and a benefit in entropy). It applies to the binding of O(2) to haemoglobin, which indeed occurs with a hitherto unreported loosening of the amide backbones of the haemoglobin monomers.

L9 ANSWER 6 OF 29 MEDLINE on STN
ACCESSION NUMBER: 2003121373 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12633996
TITLE: mRNA display: ligand discovery, interaction analysis and beyond.
AUTHOR: Takahashi Terry T; Austin Ryan J; Roberts Richard W
CORPORATE SOURCE: Department of Biochemistry and Molecular Biophysics, Pasadena, California 91125, USA.
CONTRACT NUMBER: GM01416 (NIGMS)
T32 GM08501 (NIGMS)
SOURCE: Trends in biochemical sciences, (2003 Mar) 28 (3) 159-65. Ref: 42
Journal code: 7610674. ISSN: 0968-0004.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200307
ENTRY DATE: Entered STN: 20030314
Last Updated on STN: 20030709
Entered Medline: 20030708

ED Entered STN: 20030314
Last Updated on STN: 20030709

Entered Medline: 20030708

AB In vitro peptide and protein selection using mRNA display enables the discovery and directed evolution of new molecules from combinatorial libraries. These selected molecules can serve as tools to control and understand biological processes, enhance our understanding of molecular interactions and potentially treat disease in therapeutic applications. In mRNA display, mRNA molecules are covalently attached to the peptide or protein they encode. These mRNA-protein fusions enable in vitro selection of peptide and protein libraries of >10(13) different sequences. mRNA display has been used to discover novel peptide and protein ligands for RNA, small molecules and proteins, as well as to define cellular interaction partners of proteins and drugs. In addition, several unique applications are possible with mRNA display, including self-assembling protein chips and library construction with unnatural amino acids and chemically modified peptides.

L9 ANSWER 7 OF 29 MEDLINE on STN

ACCESSION NUMBER: 2002475163 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12236771
TITLE: Photoswitching of ligand association with a photoresponsive polymer-protein conjugate.
AUTHOR: Shimoboji Tsuyoshi; Ding Zhongli L; Stayton Patrick S; Hoffman Allan S
CORPORATE SOURCE: Department of Bioengineering, University of Washington, Seattle, Washington 98195, USA.
CONTRACT NUMBER: GM53771 (NIGMS)
SOURCE: Bioconjugate chemistry, (2002 Sep-Oct) 13 (5) 915-9. Journal code: 9010319. ISSN: 1043-1802.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200306
ENTRY DATE: Entered STN: 20020919
Last Updated on STN: 20030617
Entered Medline: 20030616

ED Entered STN: 20020919
Last Updated on STN: 20030617
Entered Medline: 20030616

AB Light-regulated molecular switches that reversibly control biomolecular function could provide new opportunities for controlling activity in diagnostics, affinity separations, bioprocessing, therapeutics, and bioelectronics applications. Here we show that site-specific conjugation of light-responsive polymers near the biotin-binding pocket of streptavidin provides control of ligand binding affinity in response to UV and visible light irradiation. Two different light-responsive polymers were utilized that display opposite photoresponsive solubility changes under UV or visible (vis) light irradiation in aqueous solutions. At 40 degrees C, the N,N-dimethylacrylamide (DMA)-co-4-phenylazophenyl acrylate (AZAA) copolymer (DMAA) was soluble under UV irradiation and precipitated under visible light, while the DMA-co-N-4-phenylazophenyl acrylamide (AZAAm) copolymer (DMAAm) was soluble under visible irradiation and precipitated under UV light. Both polymers were synthesized with a vinyl sulfone terminus and

conjugated to the Glu116Cys (E116C) streptavidin mutant via thiol coupling. The DMAA-streptavidin conjugate bound biotin efficiently when the polymer was in the soluble state under UV irradiation, but under visible irradiation, the polymer collapsed and blocked free biotin association. Furthermore, if biotin was allowed to bind when the polymer was in the soluble state under UV irradiation, then when the polymer was collapsed by visible light, the streptavidin released the bound biotin. The DMAAm-streptavidin conjugate showed the opposite response, with association of biotin allowed under visible light irradiation and blocked under UV irradiation. The photoresponses of the streptavidin conjugates thus correspond to the original photoresponsive phase transition properties of the polymer switches triggered by the cis-trans isomerization of the diazo chromophores.

L9 ANSWER 8 OF 29 MEDLINE on STN
ACCESSION NUMBER: 2002452988 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12209796
TITLE: Screening for peptide affinity ligands on CIM monoliths.
AUTHOR: Pflegerl K; Podgornik A; Berger E; Jungbauer A
CORPORATE SOURCE: Institute of Applied Microbiology, University of Agricultural Sciences, Muthgasse 18, Vienna, Austria.
SOURCE: Biotechnology and bioengineering, (2002 Sep 30) 79 (7) 733-40.
Journal code: 7502021. ISSN: 0006-3592.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200302
ENTRY DATE: Entered STN: 20020906
Last Updated on STN: 20030214
Entered Medline: 20030212

ED Entered STN: 20020906
Last Updated on STN: 20030214
Entered Medline: 20030212

AB Screening of peptide ligands for affinity chromatography usually involves incubation with the target protein in a batch system. In an additional step, peptides with fast binding kinetics have to be selected in respect to satisfactory performance under flow conditions on a support ensuring optimal three-dimensional presentation of the peptide. We have developed a rapid screening system based on peptide synthesis and screening on CIM((R)) disks. The disk size was minimized to fit into microplates usually applied for solid-phase extraction. In combination with a vacuum manifold, semi-automated peptide synthesis and screening for binding to a target protein under simulated chromatography conditions are possible. Various analytical methods can be applied for parallel and automated determination of the quantity, integrity, or activity of the target protein in the flow through or bound to the affinity support. This system also allows parallel screening for suitable chromatographic conditions like running buffer, washing, and elution conditions.

L9 ANSWER 9 OF 29 MEDLINE on STN
ACCESSION NUMBER: 2002311430 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12053739
TITLE: Scanning force microscopy studies on the structure and dynamics of single DNA molecules.
AUTHOR: Zuccheri Giampaolo; Samori Bruno
CORPORATE SOURCE: Department of Biochemistry, University of Bologna, 40126 Bologna, Italy.
SOURCE: Methods in cell biology, (2002) 68 357-95.
Journal code: 0373334. ISSN: 0091-679X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200301
ENTRY DATE: Entered STN: 20020611
Last Updated on STN: 20030202
Entered Medline: 20030131
ED Entered STN: 20020611
Last Updated on STN: 20030202
Entered Medline: 20030131

L9 ANSWER 10 OF 29 MEDLINE on STN
ACCESSION NUMBER: 2002222557 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11959797
TITLE: Direct visualization of ligand-protein interactions using atomic force microscopy.
AUTHOR: Neish Calum S; Martin Ian L; Henderson Robert M; Edwardson J Michael
CORPORATE SOURCE: Department of Pharmacology, University of Cambridge, Cambridge CB2 1PD, UK.
SOURCE: British journal of pharmacology, (2002 Apr) 135 (8) 1943-50.
Journal code: 7502536. ISSN: 0007-1188.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200209
ENTRY DATE: Entered STN: 20020418
Last Updated on STN: 20020918
Entered Medline: 20020917
ED Entered STN: 20020418
Last Updated on STN: 20020918
Entered Medline: 20020917
AB 1. Streptavidin is a 60-kDa tetramer which binds four molecules of biotin with extremely high affinity (K(A) approximately 10(14) M(-1)). We have used atomic force microscopy (AFM) to visualize this ligand-protein interaction directly. 2. Biotin was tagged with a short (152-basepair; 50-nm) DNA rod and incubated with streptavidin. The resulting complexes were then imaged by AFM. The molecular volume of streptavidin calculated from the dimensions of the protein particles (105+/-3 nm(3)) was in close agreement with the value calculated from its molecular mass (114 nm(3)). Biotinylation increased the apparent size of streptavidin (to 133+/-2 nm(3)), concomitant with an increase in the thermal

stability of the tetramer. 3. Images of streptavidin with one to four molecules of DNA-biotin bound were obtained. When two ligands were bound, the angle between the DNA rods was either acute or obtuse, as expected from the relative orientations of the biotin binding sites. The ratio of acute : obtuse angles (1 : 3) was lower than the expected value (1 : 2), indicating a degree of steric hindrance in the binding of the DNA-biotin. The slight under-representation of higher occupancy states supported this idea. 4. Streptavidin with a single molecule of DNA-biotin bound was used to tag biotinylated beta-galactosidase, a model multimeric enzyme. 5. The ability to image directly the binding of a ligand to its protein target by AFM provides useful information about the nature of the interaction, and about the effect of complex formation on the structure of the protein. Furthermore, the use of DNA-biotin/streptavidin tags could potentially shed light on the architecture of multi-subunit proteins.

L9 ANSWER 11 OF 29 MEDLINE on STN
ACCESSION NUMBER: 2002200220 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11933066
TITLE: Contributions to the binding free energy of ligands to avidin and streptavidin.
AUTHOR: Lazaridis Themis; Masunov Artem; Gandolfo Francois
CORPORATE SOURCE: Department of Chemistry, City College of the City University of New York, New York, New York 10031, USA.. themis@sci.ccny.cuny.edu
SOURCE: Proteins, (2002 May 1) 47 (2) 194-208. Journal code: 8700181. ISSN: 1097-0134.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200204
ENTRY DATE: Entered STN: 20020405
Last Updated on STN: 20020424
Entered Medline: 20020423

ED Entered STN: 20020405
Last Updated on STN: 20020424
Entered Medline: 20020423

AB The free energy of binding of a ligand to a macromolecule is here formally decomposed into the (effective) energy of interaction, reorganization energy of the ligand and the macromolecule, conformational entropy change of the ligand and the macromolecule, and translational and rotational entropy loss of the ligand. Molecular dynamics simulations with implicit solvation are used to evaluate these contributions in the binding of biotin, biotin analogs, and two peptides to avidin and streptavidin. We find that the largest contribution opposing binding is the protein reorganization energy, which is calculated to be from 10 to 30 kcal/mol for the ligands considered here. The ligand reorganization energy is also significant for flexible ligands. The translational/rotational entropy is 4.5-6 kcal/mol at 1 M standard state and room temperature. The calculated binding free energies are in the correct range, but the large statistical uncertainty in the protein reorganization energy precludes precise predictions. For some complexes, the simulations show multiple binding modes,

different from the one observed in the crystal structure. This finding is probably due to deficiencies in the force field but may also reflect considerable ligand flexibility.

L9 ANSWER 12 OF 29 MEDLINE on STN
ACCESSION NUMBER: 2001464881 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11509722
TITLE: Nanowire nanosensors for highly sensitive and selective detection of biological and chemical species.
AUTHOR: Cui Y; Wei Q; Park H; Lieber C M
CORPORATE SOURCE: Department of Chemistry and Chemical Biology, Harvard University, Cambridge, MA 02138, USA.
SOURCE: Science, (2001 Aug 17) 293 (5533) 1289-92.
Journal code: 0404511. ISSN: 0036-8075.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 20010820
Last Updated on STN: 20010910
Entered Medline: 20010906

ED Entered STN: 20010820
Last Updated on STN: 20010910
Entered Medline: 20010906

AB Boron-doped silicon nanowires (SiNWs) were used to create highly sensitive, real-time electrically based sensors for biological and chemical species. Amine- and oxide-functionalized SiNWs exhibit pH-dependent conductance that was linear over a large dynamic range and could be understood in terms of the change in surface charge during protonation and deprotonation. Biotin-modified SiNWs were used to detect streptavidin down to at least a picomolar concentration range. In addition, antigen-functionalized SiNWs show reversible antibody binding and concentration-dependent detection in real time. Lastly, detection of the reversible binding of the metabolic indicator Ca2+ was demonstrated. The small size and capability of these semiconductor nanowires for sensitive, label-free, real-time detection of a wide range of chemical and biological species could be exploited in array-based screening and in vivo diagnostics.

L9 ANSWER 13 OF 29 MEDLINE on STN
ACCESSION NUMBER: 2001429235 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11476539
TITLE: Automatic Edman microsequencing of peptides containing multiple unnatural amino acids.
AUTHOR: Liu R; Lam K S
CORPORATE SOURCE: Division of Hematology and Oncology, Department of Internal Medicine, UC Davis Cancer Center, University of California, Davis, 4501 X Street, Sacramento, California 95817, USA.
CONTRACT NUMBER: 78909 (NCI)
86364
CA78868

SOURCE: Analytical biochemistry, (2001 Aug 1) 295 (1) 9-16.
Journal code: 0370535. ISSN: 0003-2697.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200110
ENTRY DATE: Entered STN: 20011022
Last Updated on STN: 20011022
Entered Medline: 20011018

ED Entered STN: 20011022
Last Updated on STN: 20011022
Entered Medline: 20011018

AB It is now routine using automatic Edman microsequencing to determine the primary structure of peptides or proteins containing natural amino acids; however, a deficiency in the ability to readily sequence peptides containing unnatural amino acids remains. With the advent of synthetic peptide chemistry, combinatorial chemistry, and the large number of commercially available unnatural amino acids, there is a need for efficient and accurate structure determination of short peptides containing many unnatural amino acids. In this study, 35 commercially available alpha-unnatural amino acids were selected to determine their elution profile on an ABI protein sequencer. Using a slightly modified gradient program, 19 of these 35 PTH amino acids can be readily resolved and distinguished from common PTH amino acids at low picomole levels. These unnatural amino acids in conjunction with the 20 natural amino acids can be used as building blocks to construct peptide libraries, and peptide beads isolated from these libraries can be readily microsequenced. To demonstrate this, we synthesized a simple tripeptide "one-bead one-compound" combinatorial library containing 14 unnatural and 19 natural amino acids and screened this library for streptavidin-binding ligands. Microsequencing of the isolated peptide-beads revealed the novel motif Bpa-Phe(4-X)-Aib, wherein X = H, OH, and CH3.

L9 ANSWER 14 OF 29 MEDLINE on STN
ACCESSION NUMBER: 2001026266 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11017049
TITLE: Detecting protein analytes that modulate transmembrane movement of a polymer chain within a single protein pore.
COMMENT: Comment in: Nat Biotechnol. 2000 Oct;18(10):1037.
PubMed ID: 11017035
AUTHOR: Movileanu L; Howorka S; Braha O; Bayley H
CORPORATE SOURCE: Department of Medical Biochemistry and Genetics, The Texas A&M University System Health Science Center, College Station, TX 77843-1114, USA.
SOURCE: Nature biotechnology, (2000 Oct) 18 (10) 1091-5.
Journal code: 9604648. ISSN: 1087-0156.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200011

ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001115

ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001115

AB Here we describe a new type of biosensor element for detecting proteins in solution at nanomolar concentrations. We tethered a 3.4 kDa polyethylene glycol chain at a defined site within the lumen of the transmembrane protein pore formed by staphylococcal alpha-hemolysin. The free end of the polymer was covalently attached to a biotin molecule. On incorporation of the modified pore into a lipid bilayer, the biotinyl group moves from one side of the membrane to the other, and is detected by reversible capture with a mutant streptavidin. The capture events are observed as changes in ionic current passing through single pores in planar bilayers. Accordingly, the modified pore allows detection of a protein analyte at the single-molecule level, facilitating both quantification and identification through a distinctive current signature. The approach has higher time resolution compared with other kinetic measurements, such as those obtained by surface plasmon resonance.

L9 ANSWER 15 OF 29 MEDLINE on STN
ACCESSION NUMBER: 2001026252 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11017035
TITLE: Sensing proteins outside of the box.
COMMENT: Comment on: Nat Biotechnol. 2000 Oct;18(10):1091-5.
PubMed ID: 11017049
AUTHOR: van der Goot F G; Matile S
SOURCE: Nature biotechnology, (2000 Oct) 18 (10) 1037.
Journal code: 9604648. ISSN: 1087-0156.
PUB. COUNTRY: United States
DOCUMENT TYPE: Commentary
News Announcement
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200011
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001115

ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001115

L9 ANSWER 16 OF 29 MEDLINE on STN
ACCESSION NUMBER: 2000327304 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10866975
TITLE: Synchrotron radiation diffraction from two-dimensional protein crystals at the air/water interface.
AUTHOR: Lenne P F; Berge B; Renault A; Zakri C; Venien-Bryan C; Courty S; Balavoine F; Bergsma-Schutter W; Brisson A; Grubel G; Boudet N; Konovalov O; Legrand J F
CORPORATE SOURCE: Laboratoire de Spectrometrie Physique, UMR Centre National de la Recherche Scientifique-Universite J.

Fourier, 38041 Grenoble, France.
SOURCE: Biophysical journal, (2000 Jul) 79 (1) 496-500.
Journal code: 0370626. ISSN: 0006-3495.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000811
Last Updated on STN: 20001019
Entered Medline: 20000803

ED Entered STN: 20000811
Last Updated on STN: 20001019
Entered Medline: 20000803

AB Protein structure determination by classical x-ray crystallography requires three-dimensional crystals that are difficult to obtain for most proteins and especially for membrane proteins. An alternative is to grow two-dimensional (2D) crystals by adsorbing proteins to ligand-lipid monolayers at the surface of water. This confined geometry requires only small amounts of material and offers numerous advantages: self-assembly and ordering over micrometer scales is easier to obtain in two dimensions; although fully hydrated, the crystals are sufficiently rigid to be investigated by various techniques, such as electron crystallography or micromechanical measurements. Here we report structural studies, using grazing incidence synchrotron x-ray diffraction, of three different 2D protein crystals at the air-water interface, namely streptavidine, annexin V, and the transcription factor HupR. Using a set-up of high angular resolution, we observe narrow Bragg reflections showing long-range crystalline order in two dimensions. In the case of streptavidin the angular range of the observed diffraction corresponds to a resolution of 10 A in plane and 14 A normal to the plane. We show that this approach is complementary to electron crystallography but without the need for transfer of the monolayer onto a grid. Moreover, as the 2D crystals are accessible from the buffer solution, the formation and structure of protein complexes can be investigated in situ.

L9 ANSWER 17 OF 29 MEDLINE on STN
ACCESSION NUMBER: 2000147366 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10683742
TITLE: PNA-dependent gene chemistry: stable coupling of peptides and oligonucleotides to plasmid DNA.
AUTHOR: Zelphati O; Liang X; Nguyen C; Barlow S; Sheng S; Shao Z; Felgner P L
CORPORATE SOURCE: Gene Therapy Systems, San Diego, CA, USA.
CONTRACT NUMBER: 1R44CA80598 (NCI)
RR07720 (NCRR)
SOURCE: BioTechniques, (2000 Feb) 28 (2) 304-10, 312-4, 316.
Journal code: 8306785. ISSN: 0736-6205.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000407

Last Updated on STN: 20000407
Entered Medline: 20000330

ED Entered STN: 20000407
Last Updated on STN: 20000407
Entered Medline: 20000330

AB Two approaches are described for stably conjugating peptides, proteins and oligonucleotides onto plasmid DNA. Both methods use a peptide nucleic acid (PNA) clamp, which binds irreversibly and specifically to a binding site cloned into the plasmid. The first approach uses a biotin-conjugated PNA clamp that can be used to introduce functional biotin groups onto the plasmid to which streptavidin can bind. Atomic force microscopy images of linearized plasmid show streptavidin localized at the predicted PNA binding site on the DNA strand. Peptides and oligonucleotides containing free thiol groups were conjugated to maleimide streptavidin, and these streptavidin conjugates were bound to the biotin-PNA-labeled plasmid. In this way, peptides and oligonucleotides could be brought into stable association with the plasmid. A second approach used a maleimide-conjugated PNA clamp. Methods are described for conjugating thiolated peptides and oligonucleotides directly to the maleimide-PNA-DNA hybrid. This straightforward technology offers an easy approach to introduce functional groups onto plasmid DNA without disturbing its transcriptional activity.

L9 ANSWER 18 OF 29 MEDLINE on STN
ACCESSION NUMBER: 1999309314 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10380216
TITLE: Thermodynamics and kinetics of ligand-protein binding studied with the weighted histogram analysis method and simulated annealing.
AUTHOR: Bouzida D; Arthurs S; Colson A B; Freer S T; Gehlhaar D K; Larson V; Luty B A; Rejto P A; Rose P W; Verkhivker G M
CORPORATE SOURCE: Agouron Pharmaceuticals, Inc., La Jolla, CA 92037-1022, USA.
SOURCE: Pacific Symposium on Biocomputing. Pacific Symposium on Biocomputing, (1999) 426-37.
Journal code: 9711271.
PUB. COUNTRY: Singapore
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990820
Last Updated on STN: 19990820
Entered Medline: 19990810

ED Entered STN: 19990820
Last Updated on STN: 19990820
Entered Medline: 19990810

AB The thermodynamics of ligand-protein molecular recognition is investigated by the energy landscape approach for two systems: methotrexate(MTX)--dihydrofolate reductase(DHFR) and biotin-streptavidin. The temperature-dependent binding free energy profile is determined using the weighted histogram analysis method. Two different force fields are employed in this study: a simplified model of ligand-protein interactions and the AMBER force field with

a soft core smoothing component, used to soften the repulsive part of the potential. The results of multiple docking simulations are rationalized from the shape of the binding free energy profile that characterizes the thermodynamics of the binding process.

L9 ANSWER 19 OF 29 MEDLINE on STN
ACCESSION NUMBER: 1999188594 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10090208
TITLE: Microscopy for recognition of individual biomolecules.
AUTHOR: Schmidt T; Hinterdorfer P; Schindler H
CORPORATE SOURCE: Institute for Biophysics, University of Linz, Austria.
SOURCE: Microscopy research and technique, (1999 Mar 1) 44 (5) 339-46.
Journal code: 9203012. ISSN: 1059-910X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199907
ENTRY DATE: Entered STN: 19990816
Last Updated on STN: 19990816
Entered Medline: 19990730
ED Entered STN: 19990816
Last Updated on STN: 19990816
Entered Medline: 19990730
AB One frontier challenge in microscopy and analytical chemistry is the analysis of soft matter at the single molecule level with biological systems as most complex examples. Towards this goal we have developed two novel microscopy methods. Both employ highly specific molecular recognition schemes used by nature-the recognition of specific protein sites by antibodies and ligands. One method uses fluorescence labeled ligands for detecting single molecules in fluid systems like membranes (Fig. 1B). Unitary signals are reliably resolved even for millisecond illumination periods. The knowledge of the unitary signal from single molecules permits the determination of stoichiometries of component association (Fig. 3). Direct imaging of the diffusional path of single molecules became possible for the first time (Fig. 4). Using linear polarized excitation, the angular orientation of single molecules can be analyzed (single molecule linear dichroism, (Fig. 5), which opens a new perspective for detecting conformational changes of single biomolecules. In the other method, an antibody is flexibly linked to the tip of an atomic-force microscope. This permits the identification of receptors in multi-component systems. Molecular mapping of biosurfaces and the study of molecular dynamics in the ms to s range become possible with atomic force microscopy.

L9 ANSWER 20 OF 29 MEDLINE on STN
ACCESSION NUMBER: 1999107365 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9892347
TITLE: Biophysics. May the force be with you.
COMMENT: Comment on: Nature. 1999 Jan 7;397(6714):50-3. PubMed ID: 9892352
AUTHOR: Stayton P S

SOURCE: Nature, (1999 Jan 7) 397 (6714) 20-1.
Journal code: 0410462. ISSN: 0028-0836.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Commentary
News Announcement
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199902
ENTRY DATE: Entered STN: 19990216
Last Updated on STN: 19990216
Entered Medline: 19990201
ED Entered STN: 19990216
Last Updated on STN: 19990216
Entered Medline: 19990201

L9 ANSWER 21 OF 29 MEDLINE on STN
ACCESSION NUMBER: 1999079327 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9863623
TITLE: Functional analysis of GnRH receptor ligand binding using biotinylated GnRH derivatives.
AUTHOR: Byrne B; Klahn S; Taylor P L; Eidne K A
CORPORATE SOURCE: MRC Reproductive Biology Unit, Edinburgh, UK.
SOURCE: Molecular and cellular endocrinology, (1998 Sep 25) 144 (1-2) 11-9.
Journal code: 7500844. ISSN: 0303-7207.
PUB. COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199903
ENTRY DATE: Entered STN: 19990316
Last Updated on STN: 19990316
Entered Medline: 19990301
ED Entered STN: 19990316
Last Updated on STN: 19990316
Entered Medline: 19990301
AB The objective of this study was to determine whether the gonadotrophin-releasing hormone (GnRH) ligand binds to the GnRH receptor (GnRH-R) with either the N- and C-termini or the beta-II turn pointing towards the cell. The functionality of GnRH and two biotinylated GnRH derivatives, biotin [D-Lys6]GnRH and biotin [Gln1]GnRH biotinylated at positions 6 and 1, respectively was assessed. Streptavidin was also used in combination with these peptides to investigate the effects of the steric hindrance caused by this molecule on ligand binding when bound to the biotin molecules at the two positions. GnRH bound to the receptor with high affinity, which was not affected by the addition of streptavidin. Both the biotinylated derivatives bound to the receptor though with lower affinities than GnRH. The biotin [D-Lys6]GnRH-streptavidin complex bound to the receptor albeit with lower affinity compared to biotin [D-Lys6]GnRH only, although it maintained its ability to cause receptor internalisation. The ability of the biotin [Gln1]GnRH to bind to the receptor was abolished in the presence of excess streptavidin. Both GnRH and biotin [D-Lys6]GnRH stimulated total inositol phosphate production whereas biotin [Gln1]GnRH exhibited GnRH antagonist activity. It

appears that the small biotin molecule can be accommodated within the binding pore when attached to position 1 of the ligand but not when complexed to streptavidin. The fact that biotin [D-Lys6]GnRH maintains functionality when complexed to streptavidin while biotin [Gln1]GnRH does not, suggests that the N- and possibly the C-termini are required for receptor binding. Thus the most likely binding orientation for the ligand is with the N- and C-termini pointing inwards with the residue at position 6 pointing away from the binding site.

L9 ANSWER 22 OF 29 MEDLINE on STN
ACCESSION NUMBER: 97381301 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9238633
TITLE: Design considerations and computer modeling related to the development of molecular scaffolds and peptide mimetics for combinatorial chemistry.
AUTHOR: Hruby V J; Shenderovich M; Lam K S; Lebl M
CORPORATE SOURCE: Department of Chemistry, University of Arizona, Tucson 85721, USA.
CONTRACT NUMBER: CA27502 (NCI)
DA06284 (NIDA)
SOURCE: Molecular diversity, (1996 Oct) 2 (1-2) 46-56.
Journal code: 9516534. ISSN: 1381-1991.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199708
ENTRY DATE: Entered STN: 19970902
Last Updated on STN: 19980206
Entered Medline: 19970821
ED Entered STN: 19970902
Last Updated on STN: 19980206
Entered Medline: 19970821
AB A critical issue in drug discovery utilizing combinatorial chemistry as part of the discovery process is the choice of scaffolds to be used for a proper presentation, in a three-dimensional space, of the critical elements of structure necessary for molecular recognition (binding) and information transfer (agonist/ antagonist). In the case of polypeptide ligands, considerations related to the properties of various backbone structures (alpha-helix, beta-sheets, etc.; phi, psi space) and those related to three-dimensional presentation of side-chain moieties (topography; chi (chi) space) must be addressed, although they often present quite different elements in the molecular recognition puzzle. We have addressed aspects of this problem by examining the three-dimensional structures of chemically different scaffolds at various distances from the scaffold to evaluate their putative diversity. We find that chemically diverse scaffolds can readily become topographically similar. We suggest a topographical approach involving design in chi space to deal with these problems.

L9 ANSWER 23 OF 29 MEDLINE on STN
ACCESSION NUMBER: 97294734 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9148939
TITLE: In crystals of complexes of streptavidin with peptide

ligands containing the HPQ sequence the pKa of the peptide histidine is less than 3.0.

AUTHOR: Katz B A; Cass R T
CORPORATE SOURCE: Arris Pharmaceutical Corporation, South San Francisco, California 94080, USA.. bak@arris.com

SOURCE: Journal of biological chemistry, (1997 May 16) 272 (20) 13220-8.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199706
ENTRY DATE: Entered STN: 19970630
Last Updated on STN: 19980206
Entered Medline: 19970619

ED Entered STN: 19970630
Last Updated on STN: 19980206
Entered Medline: 19970619

AB The pH dependences of the affinities for streptavidin of linear and cyclic peptide ligands containing the HPQ sequence discovered by phage display were determined by plasmon resonance measurements. At pH values ranging from 3.0 to 9.0, the Kd values for Ac-AEFSHPQNTIEGRK-NH2, cyclo-Ac-AE[CHPQGPPC]IEGRK-NH2, and cyclo-Ac-AE[CHPQFC]IEGRK-NH2, were determined by competition, and those for cyclo-[5-S-valeramide-HPQGPPC]K-NH2 were determined directly by equilibrium affinity measurements. The Kd values of the ligands increase by an average factor of 3.0 +/- 0.8 per decrease in pH unit between pH approximately 4.5 and pH approximately 6.3. Below pH approximately 4.5 there is a smaller increase in Kd values, and above pH approximately 6.3 the Kd values become relatively pH-independent. We determined the crystal structures of complexes of streptavidin with cyclo-[5-S-valeramide-HPQGPPC]K-NH2 at pH 1.5, 2.5, 3.0, and 3.5, with cyclo-Ac-[CHPQFC]-NH2 at pH 2.0, 3.0, 3.6, 4.2, 4.8, and 11.8, with cyclo-Ac-[CHPQGPPC]-NH2 at pH 2.5, 2.9, and 3.7, and with FSHPQNT at pH 4.0 and compared the structures with one another and with those previously determined at other pH values. At pH values from 3.0 to 11.8, the electron density for the peptide His side chain is strong, flat, and well defined. A hydrogen bond between the Ndelta1 atom of the His and the peptide Gln amide group indicates the His of the bound peptide in the crystals is uncharged at pH >/= 3.0. By determining selected structures in two different space groups, I222 with two crystallographically inequivalent ligand sites and I4122 with one site, we show that below pH approximately 3.0, the pKa of the bound peptide His in the crystals is influenced by crystal packing interactions. The presence of the Ndelta1His-NGln hydrogen bond along with pH dependences of the peptide affinities suggest that deprotonation of the peptide His is required for high affinity binding of HPQ-containing peptides to streptavidin both in the crystals and in solution.

L9 ANSWER 24 OF 29 MEDLINE on STN
ACCESSION NUMBER: 97109372 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8951652
TITLE: Scoring noncovalent protein-ligand interactions: a continuous differentiable function tuned to compute

binding affinities.
AUTHOR: Jain A N
CORPORATE SOURCE: Arris Pharmaceutical Corporation, San Francisco, CA 94080, USA.
SOURCE: Journal of computer-aided molecular design, (1996 Oct) 10 (5) 427-40.
Journal code: 8710425. ISSN: 0920-654X.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 19970414
Last Updated on STN: 19980206
Entered Medline: 19970328

ED Entered STN: 19970414
Last Updated on STN: 19980206
Entered Medline: 19970328

AB Exploitation of protein structures for potential drug leads by molecular docking is critically dependent on methods for scoring putative protein-ligand interactions. An ideal function for scoring must exhibit predictive accuracy and high computational speed, and must be tolerant of variations in the relative protein-ligand molecular alignment and conformation. This paper describes the development of an empirically derived scoring function, based on the binding affinities of protein-ligand complexes coupled with their crystallographically determined structures. The function's primary terms involve hydrophobic and polar complementarity, with additional terms for entropic and solvation effects. The issue of alignment/conformation dependence was solved by constructing a continuous differentiable nonlinear function with the requirement that maxima in ligand conformation/alignment space corresponded closely to crystallographically determined structures. The expected error in the predicted affinity based on cross-validation was 1.0 log unit. The function is sufficiently fast and accurate to serve as the objective function of a molecular-docking search engine. The function is particularly well suited to the docking problem, since it has spatially narrow maxima that are broadly accessible via gradient descent.

L9 ANSWER 25 OF 29 MEDLINE on STN
ACCESSION NUMBER: 96323963 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8727324
TITLE: Molecular docking using surface complementarity.
AUTHOR: Sobolev V; Wade R C; Vriend G; Edelman M
CORPORATE SOURCE: Department of Plant Genetics, Weizmann Institute of Science, Rehovot, Israel.
SOURCE: Proteins, (1996 May) 25 (1) 120-9.
Journal code: 8700181. ISSN: 0887-3585.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199611
ENTRY DATE: Entered STN: 19961219
Last Updated on STN: 19980206

Searcher : Shears 571-272-2528

Entered Medline: 19961105

ED Entered STN: 19961219
Last Updated on STN: 19980206
Entered Medline: 19961105

AB A method is described to dock a ligand into a binding site in a protein on the basis of the complementarity of the intermolecular atomic contacts. Docking is performed by maximization of a complementarity function that is dependent on atomic contact surface area and the chemical properties of the contacting atoms. The generality and simplicity of the complementarity function ensure that a wide range of chemical structures can be handled. The ligand and the protein are treated as rigid bodies, but displacement of a small number of residues lining the ligand binding site can be taken into account. The method can assist in the design of improved ligands by indicating what changes in complementarity may occur as a result of the substitution of an atom in the ligand. The capabilities of the method are demonstrated by application to 14 protein-ligand complexes of known crystal structure.

L9 ANSWER 26 OF 29 MEDLINE on STN
ACCESSION NUMBER: 95182175 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7876904
TITLE: On the use of LUDI to search the Fine Chemicals Directory for ligands of proteins of known three-dimensional structure.
AUTHOR: Bohm H J
CORPORATE SOURCE: BASF AG, Ludwigshafen, Germany.
SOURCE: Journal of computer-aided molecular design, (1994 Oct) 8 (5) 623-32.
Journal code: 8710425. ISSN: 0920-654X.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199503
ENTRY DATE: Entered STN: 19950419
Last Updated on STN: 19980206
Entered Medline: 19950331

ED Entered STN: 19950419
Last Updated on STN: 19980206
Entered Medline: 19950331

AB It is shown that the computer program LUDI can be used to search large database of three-dimensional structures for putative ligands of proteins with known 3D structure. As an example, a subset of approximately 30,000 small molecules (with less than 40 atoms and 0-2 rotatable bonds) from the Fine Chemicals Directory has been used in the search for possible novel ligands for four different proteins (trypsin, streptavidin, purine nucleoside phosphorylase and HIV protease). For trypsin and streptavidin, known ligands or substructures of known ligands are retrieved as top-scoring hits. In addition, a number of new interesting structures are found in all considered cases. Therefore, the method holds promise to retrieve automatically protein ligands from a 3D database if the 3D structure of the target protein is known.

L9 ANSWER 27 OF 29 MEDLINE on STN

ACCESSION NUMBER: 95068954 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7978287
TITLE: The use of biotinylated poly(ADP-ribose) for studies on poly(ADP-ribose)-protein interaction.
AUTHOR: Narendja F M; Sauermann G
CORPORATE SOURCE: Institute of Tumorbiology--Cancer Research, University of Vienna, Austria.
SOURCE: Analytical biochemistry, (1994 Aug 1) 220 (2) 415-9. Journal code: 0370535. ISSN: 0003-2697.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199412
ENTRY DATE: Entered STN: 19950110
Last Updated on STN: 19980206
Entered Medline: 19941228
ED Entered STN: 19950110
Last Updated on STN: 19980206
Entered Medline: 19941228
AB Poly(ADP-ribose) is routinely detected by the use of radioactive polymers formed from labeled substrates. In this report a simple and time-saving method for the biotinylation and the detection of poly(ADP-ribose) on blots is described. The polymer modified by light-induced reaction with photobiotin was colorimetrically detected and quantified, using streptavidine-alkaline phosphatase conjugates. The separation of poly(ADP-ribose) chains on polyacrylamide gels was not affected by the biotinylation of the polymers. When biotinylated poly(ADP-ribose) was used to detect the poly(ADP-ribose) binding capability of proteins in ligand blots, the results were comparable to those obtained with poly([32P]ADP-ribose). Experiments with histones and rat liver nuclear proteins demonstrate that in studies on poly(ADP-ribose)-protein interaction, this method is applicable to the detection of poly(ADP-ribose) binding proteins.

L9 ANSWER 28 OF 29 MEDLINE on STN
ACCESSION NUMBER: 95034839 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7947806
TITLE: Effect of conformational flexibility and solvation on receptor-ligand binding free energies.
AUTHOR: Vajda S; Weng Z; Rosenfeld R; DeLisi C
CORPORATE SOURCE: Department of Biomedical Engineering, Boston University, Massachusetts 02215.
CONTRACT NUMBER: AI30535 (NIAID)
SOURCE: Biochemistry, (1994 Nov 29) 33 (47) 13977-88. Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199412
ENTRY DATE: Entered STN: 19950110
Last Updated on STN: 20000303
Entered Medline: 19941228
ED Entered STN: 19950110

Last Updated on STN: 20000303
Entered Medline: 19941228

AB A coherent framework is presented for determining the free energy change accompanying ligand binding to protein receptors. The most important new feature of the method is the contribution of the flexibility of the free ligand, and hence its conformational change on binding, to the free energy. Flexibility introduces two additional terms in the free energy difference: the internal energy difference between the ligand in the bound and free states and the backbone entropy loss. The former requires taking explicit account of the difference in solvation of the various forms of the free ligand. The solvation free energy change is estimated using an atomic solvation parameter model [Eisenberg & Mclachlan (1986) Nature 319, 199-203], with an improved parameter set. In order to evaluate the method, we applied it to three data sets for which increasingly general methods are required. The set to which the most restrictive theory can be applied consists of eight crystallized endopeptidase--protein inhibitor complexes which do not change conformation on binding and for which the major contribution to the solvation free energy is entropic. The results are in good agreement with the measured values and somewhat better than those previously reported in the literature. The second data set compares the relative binding free energies of biotin and its analogs for streptavidin. In this case the structures are also rigid, but solvation free energy must include both enthalpic and entropic components. We find that differential free energy predictions are approximately the same as those obtained by free energy perturbation techniques. The final application is an analysis of the measured stabilities of 13 different MHC receptor-peptide complexes. In this case we show that flexibility contributes 30-50% of the free energy change and find a correlation of 0.88 between our predicted free energies and peptide dissociation times.

L9 ANSWER 29 OF 29 MEDLINE on STN
ACCESSION NUMBER: 93391363 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8378312
TITLE: What determines the strength of noncovalent association of ligands to proteins in aqueous solution?.
AUTHOR: Miyamoto S; Kollman P A
CORPORATE SOURCE: Department of Pharmaceutical Chemistry, University of California, San Francisco 94143.
CONTRACT NUMBER: GM-29072 (NIGMS)
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1993 Sep 15) 90 (18) 8402-6.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199310
ENTRY DATE: Entered STN: 19931105
Last Updated on STN: 19980206
Entered Medline: 19931020
ED Entered STN: 19931105

Last Updated on STN: 19980206
Entered Medline: 19931020

AB Free energy perturbation methods using molecular dynamics have been used to calculate the absolute free energy of association of two ligand-protein complexes. The calculations reproduce the significantly more negative free energy of association of biotin to streptavidin, compared to N-L-acetyltryptophanamide/alpha-chymotrypsin. This difference in free energy of association is due to van der Waals/dispersion effects in the nearly ideally performed cavity that streptavidin presents to biotin, which involves four tryptophan residues.

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